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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
BAUM, STUART F	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 04/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/675,208	OSUMI ET AL.	
	Examiner	Art Unit	
	Stuart F. Baum	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 October 2003 and 04 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *70-120* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *70-120* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 September 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 08/846234.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The amendments filed on 10/23/2003 and 12/4/2003 have been entered.

Claims 70-120 are pending.

Claims 1-69 have been canceled.

Claims 70-120 have been newly added.

2. Claims 70-120 are examined in the present office action.

3. Rejections and objections not set forth below are withdrawn.

4. The text of those sections of Title 35, U.S. Code not included in this office action can be found in a prior office action.

Claim Objections

5. Claims 79, 84, 103 and 108, line 2, are objected to for placing a period (.) after the word "Cruciferae" instead of a comma (,).

Written Description

6. Claims 70-120 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to an isolated DNA coding for a polypeptide which comprises the amino acid sequence of SEQ ID NO:1, 2, or 3, a vector comprising said isolated DNA and plant

transformed therewith, a plant transformed with the isolated DNA, a host cell transformed with said isolated DNA and method of producing said polypeptide, a chimeric gene comprising said isolated DNA operably linked to a transcription regulatory region expressible in plant cells and plant transformed therewith, a method of modifying the content of raffinose family oligosaccharides in a plant comprising transforming a plant with said chimeric gene, an isolated DNA molecule encoding a polypeptide having an ability to produce raffinose from sucrose and galactinol wherein the DNA hybridizes under stringent conditions to nucleotide numbers 56 to 2407 of SEQ ID NO:4 and vector, plant, host cell, method of modifying the content of raffinose family oligosaccharides in a plant and method of producing a polypeptide, comprising said DNA molecule.

Applicants only disclose a raffinose synthase nucleic acid sequence from cucumber of SEQ ID NO:4 encoding SEQ ID NO:5 (page 60, lines 10-24). Applicants also disclose SEQ ID NO:1, 2, and 3 that are amino acid oligomers consisting of 30, 19 and 14 amino acids, respectively, that are part of the raffinose synthase of SEQ ID NO:5 (page 12, lines 19-25).

The Applicants do not identify essential regions of a raffinose synthase protein encoded by SEQ ID NO:4 and that comprises SEQ ID NO:1 to 3, nor do Applicants describe any polynucleotide sequences that hybridize to SEQ ID NO:4 that encodes a functional raffinose synthase protein. The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In summary, the court stated that a written description of an invention requires a precise definition, one that defines the structural features of the chemical genus that distinguishes it from other

chemical structures. A definition by function does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. The court goes on to say, "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." *See University of California v. Eli Lilly and Co.*, 119 F.3d 1559; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). Applicants fail to describe a representative number of polynucleotide sequences encoding a raffinose synthase protein falling within the scope of the claimed genus of polynucleotides which hybridize to SEQ ID NO:4 or sequences which encode a raffinose synthase protein and comprise SEQ ID NO:1 to 3. Applicants only describe a single sequence of SEQ ID NO:4. Furthermore, Applicants fail to describe structural features common to members of the claimed genus of polynucleotides. Hence, Applicants fail to meet either prong of the two-prong test set forth by *Eli Lilly*. Furthermore, given the lack of description of the necessary elements essential for the raffinose synthase protein, it remains unclear what features identify an cucumber raffinose synthase protein. Since the genus of raffinose synthase proteins has not been described by specific structural features, the specification fails to provide an adequate written description to support the breath of the claims.

Applicant's arguments filed 10/23/2003 and 12/4/2003 have been fully considered but they are not persuasive.

Applicants contend that newly added claim 70 relates to an isolated DNA coding for a polypeptide which comprises the amino acid sequences of SEQ ID NO:1, 2 or 3 and that the application describes these sequences. Accordingly, Applicants contend that claim 70 and all

dependent claims which directly depend from claim 70 have fulfilled the written description requirement (page 10, last paragraph). Applicants contend that claim 101, drawn to sequences that hybridize to SEQ ID NO:4 are described because one sequence is disclosed and techniques to isolate other sequences and compare them to the isolated sequence are well known in the art (page 11, 1st full paragraph).

The Office contends that Applicants have not fulfilled the written description requirement for the reasons stated above.

Scope of Enablement

7. Claims 70-120 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of modifying raffinose content in a plant comprising transforming a plant with a chimeric gene comprising SEQ ID NO:4 operably linked to a transcription regulatory region expressible in plants to yield plants with less raffinose than plants not transformed with said chimeric gene, does not reasonably provide enablement for a method of modifying the content of raffinose family oligosaccharides in a plant comprising any isolated DNA molecule that hybridizes to SEQ ID NO:4 that encodes a protein with the characteristics as specified in claim 97 or transforming a plant with any nucleic acid encoding a polypeptide that comprises SEQ ID NO:1, 2 or 3, or Applicants are not enabled for a method of making a polypeptide comprising transforming a host cell with a nucleic acid as specified in claims 70 or 97; Applicants have not taught how one would use said isolated polypeptide. The specification does not enable any person skilled in the art to which it pertains, or with which it is

most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are drawn to an isolated DNA coding for a polypeptide which comprises the amino acid sequence of SEQ ID NO:1, 2, or 3, a vector comprising said isolated DNA and plant transformed therewith, a plant transformed with the isolated DNA, a host cell transformed with said isolated DNA and method of producing said polypeptide, a chimeric gene comprising said isolated DNA operably linked to a transcription regulatory region expressible in plant cells and plant transformed therewith, a method of modifying the content of raffinose family oligosaccharides in a plant comprising transforming a plant with said chimeric gene, an isolated DNA molecule encoding a polypeptide having an ability to produce raffinose from sucrose and galactinol wherein the DNA hybridizes under stringent conditions to nucleotide numbers 56 to 2407 of SEQ ID NO:4 and vector, plant, host cell, method of modifying the content of raffinose family oligosaccharides in a plant and method of producing a polypeptide, comprising said DNA molecule.

Applicants disclose screening a cDNA library from cucumber and isolating a DNA sequence of SEQ ID NO: 4, encoding raffinose synthase of SEQ ID NO: 5 (pages 53-60, Example 3. Raffinose synthase catalyzes the formation of raffinose from galactinol and sucrose. The cDNA encoding raffinose synthase was subcloned into a vector in a sense and antisense orientation, operably linked to the 35S promoter. Said constructs were transformed into *Arabidopsis* and subsequent transformed plants were analyzed for raffinose content. In plants harboring either orientation of the isolated raffinose synthase encoding DNA, 0.0 mg/g raffinose were detected compared to wild type whose raffinose content was 0.2 mg/g (page 65, Table 4).

The Applicants present three additional sequences SEQ ID NO's : 1, 2, and 3 which are short amino acid sequences taken from SEQ ID NO:5 which they state can be used to generate PCR primers.

The state-of-the-art is such that one of skill in the art cannot predict which nucleic acids that hybridize to SEQ ID NO:4 will encode a protein with the same activity as a protein encoded by SEQ ID NO:4. The prediction of protein structure from sequence data and, in turn, utilizing predicted structural determinations to ascertain functional aspects of the protein, is extremely complex, and the positions within the protein's sequence where amino acid substitutions can be made with a reasonable expectation of maintaining function are limited (Bowie et al, Science 247:1306-1310, 1990, see especially page 1306). Proteins may be sensitive to alterations in even a single amino acid in a sequence. For example, the replacement of a glycine residue located within the START domain of either the PHABULOSA or PHAVOLUTA protein receptor with either an alanine or aspartic acid residue, alters the sterol/lipid binding domain (McConnell et al, Nature 411 (6838):709-713, 2001, see especially page 710, left column, 2nd paragraph).

Isolating DNA fragments using stringent hybridization conditions, does not always select for DNA fragments whose contiguous nucleotide sequence is the same or nearly the same as the probe. Fourgoux-Nicol et al (1999, Plant Molecular Biology 40 :857-872) teach the isolation of a 674bp fragment using a 497bp probe incorporating stringent hybridization conditions comprising three consecutive 30 minute rinses in 2X, 1X and 0.1X SSC with 0.1% SDS at 65^0C (page 859, left column, 2nd paragraph). Fourgoux-Nicol et al also teach that the probe and isolated DNA fragment exhibited a number of sequence differences comprising a 99bp insertion within the probe and a single nucleotide gap, while the DNA fragment contained 2 single

nucleotide gaps and together the fragments contained 27 nucleotide mismatches. Taking into account the insertions, gaps and mismatches, the longest stretch of contiguous nucleotides to which the probe could hybridize consisted of 93bp of DNA (page 862, Figure 2). In the present example, the isolated fragment exhibits less than 50% sequence identity with the probe.

In the absence of guidance, undue trial and error experimentation would be required for one of ordinary skill in the art to screen through the multitude of non-exemplified sequences, either by using non-disclosed fragments of SEQ ID NO:4 as probes or by designing primers to undisclosed regions of SEQ ID NO:4 and isolating or amplifying fragments, subcloning the fragments, producing expression vectors and transforming plants therewith, in order to identify those, if any, that when over-expressed modify the content of raffinose family oligosaccharides in a plant and fall within the scope of Applicants' claims.

Therefore, given the breadth of the claims; the lack of guidance and examples; the unpredictability in the art; and the state-of-the-art as discussed above, undue experimentation would be required to practice the claimed invention, and therefore the invention is not enabled.

Applicant's arguments filed 10/23/2003 and 12/4/2003 have been fully considered but they are not persuasive.

Applicants contend that the specification provides guidance to make and use the claimed sequences, i.e., sequences comprising SEQ ID NO:1, 2, or 3 (paragraph bridging pages 10 and 11).

The Office contends, that other than SEQ ID NO:4 encoding SEQ ID NO:5, Applicants do not disclose other sequences encompassed by the claims that can be used in the present invention.

Applicants contend that the present application provides a detailed description of methods and procedures for producing a DNA within the scope of claim 101 (page 11, 1st paragraph).

Applicants do not disclose a sequence that hybridizes with SEQ ID NO:4 that can be used in the present invention.

Double Patenting

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper time wise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 70-120 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-41 of U.S. Patent No. 6,166,292 (listed in 1449). Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims are obvious over the claims of Patent No. 6166292. Claims 1-41 are drawn to an isolated DNA which originates from an organism having an ability to produce raffinose from sucrose and galactinol, with the nucleotide sequence comprising at least nucleotide residues 56 to 2407 of the nucleotide sequence of SEQ ID NO:4 and encodes a protein which has the amino acid sequence of SEQ ID NO:5 exhibiting inherent properties of an isolated raffinose synthase protein as described in Patent No. 6,166,292 column 3 last paragraph. In addition, Patent No. 6,166,292 teach SEQ ID NO:1, 2, or 3 of the present as being amino acid sequences from SEQ ID NO:5.

10. Claims 70-120 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 25-88 of copending Application No. 09/425055. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 25-88 are drawn to a DNA encoding a raffinose synthase comprising SEQ ID NO:1, 2, or 3 or a nucleic acid that hybridizes under stringent conditions to a DNA comprising nucleotide numbers 56-2407 of SEQ ID NO:4 and encodes a protein able to produce raffinose from sucrose and galactinol, a transformed plant and a method for changing the content of raffinose family oligosaccharides in a plant which reads on the same material as specified in the claims of the present application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant's arguments filed 10/23/2003 and 12/4/2003 have been fully considered but they are not persuasive.

Applicant in the response filed 10/23/2003, requests that this rejection be held in abeyance until an indication of allowable subject matter (page 11, 4th paragraph). This is granted.

11. Claims 70-120 are deemed free of the prior art, given the failure of the prior art to teach or reasonably suggest an isolated an isolated DNA coding for a polypeptide which comprises the amino acid sequence of SEQ ID NO:1, 2, or 3, a vector comprising said isolated DNA and plant transformed therewith, a plant transformed with the isolated DNA, a host cell transformed with said isolated DNA and method of producing said polypeptide, a chimeric gene comprising said isolated DNA operably linked to a transcription regulatory region expressible in plant cells and plant transformed therewith, a method of modifying the content of raffinose family oligosaccharides in a plant comprising transforming a plant with said chimeric gene, an isolated DNA molecule encoding a polypeptide having an ability to produce raffinose from sucrose and galactinol wherein the DNA hybridizes under stringent conditions to nucleotide numbers 56 to 2407 of SEQ ID NO:4 and vector, plant, host cell, method of modifying the content of raffinose family oligosaccharides in a plant and method of producing a polypeptide, comprising said DNA molecule.

12. No claims are allowed.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart F. Baum whose telephone number is 571-272-0792. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on 571-272-0804. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Stuart F. Baum Ph.D.
Patent Examiner
Art Unit 1638
April 16, 2004

ELIZABETH F. McELWAIN
PRIMARY EXAMINER
GROUP 1600